

## WEST Search History

DATE: Thursday, May 20, 2004

<b>Hide?</b>	<b>Set Name</b>	<b>Query</b>	<b>Hit Count</b>
<i>DB=USPT,PGPB,EPAB,DWPI; PLUR=YES; OP=ADJ</i>			
<input type="checkbox"/>	L1	10/071411	0
<input type="checkbox"/>	L2	10/071,411	0
<input type="checkbox"/>	L3	10071,411	1
<input type="checkbox"/>	L4	5-LO gene same allelic variant	2
<input type="checkbox"/>	L5	5-LO gene	13
<input type="checkbox"/>	L6	L5 and (polymorphism or variant or SNP)	10
<input type="checkbox"/>	L7	restriction enzyme site analysis	34
<input type="checkbox"/>	L8	single-stranded conformation polymorphism	355
<input type="checkbox"/>	L9	allele specific hybridization	400
<input type="checkbox"/>	L10	primer specific extension	45
<input type="checkbox"/>	L11	oligonucleotide ligation assay	934
<input type="checkbox"/>	L12	5-lipoxygenase gene	24
<input type="checkbox"/>	L13	L12 and L7	0
<input type="checkbox"/>	L14	L12 and L8	1
<input type="checkbox"/>	L15	L12 and L9	0
<input type="checkbox"/>	L16	L12 and L10	0
<input type="checkbox"/>	L17	L12 and L11	3
<i>DB=PGPB,USPT,EPAB,DWPI; PLUR=YES; OP=ADJ</i>			
<input type="checkbox"/>	L18	Barnes-G\$.in.	300
<input type="checkbox"/>	L19	L18 and lipoxygenase gene	1
<input type="checkbox"/>	L20	lipoxygenase gene	85
<input type="checkbox"/>	L21	5-lipoxygenase gene	24

END OF SEARCH HISTORY

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(FILE 'HOME' ENTERED AT 14:59:00 ON 20 MAY 2004)

FILE 'MEDLINE, BIOTECHDS, EMBASE, BIOSIS, SCISEARCH, CANCERLIT, CAPLUS'  
ENTERED AT 14:59:44 ON 20 MAY 2004

L1 3324 S BARNES G?/AU  
L2 909 S LIPOXYGENASE GENE  
L3 293 S 5-LIPOXYGENASE GENE  
L4 1645787 S POLYMORPHISM OR VARIANT OR SNP OR MUTATION  
L5 4 S L1 AND L2  
L6 70 S L3 AND L4  
L7 1 S L6 AND RESTRICTION ENZYME SITE  
L8 1 S L6 AND SINGLE STRANDED CONFORMATION POLYMOR?  
L9 1 S L6 AND PRIMER EXTENSION  
L10 2 S L6 AND LIGATION  
L11 3 DUP REM L5 (1 DUPLICATE REMOVED)

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L11 ANSWER 1 OF 3 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN

ACCESSION NUMBER: 2003-02110 BIOTECHDS

TITLE: New isolated nucleic acid molecule with an allelic variant of a polymorphic region of an 5-LO gene, useful for diagnosing and/or prognosticating disorders associated with an aberrant inflammatory response such as asthma;  
human recombinant 5-lipoxygenase gene  
isolation for use in disease diagnosis and prognosis

AUTHOR: BARNES G; MEYER J

PATENT ASSIGNEE: MILLENNIUM PHARM INC

PATENT INFO: WO 2002062825 15 Aug 2002

APPLICATION INFO: WO 2002-US3546 7 Feb 2002

PRIORITY INFO: US 2001-314248 21 Aug 2001; US 2001-267515 8 Feb 2001

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2002-627522 [67]

AN 2003-02110 BIOTECHDS

AB DERWENT ABSTRACT:

NOVELTY - An isolated human nucleic acid molecule (I) comprising an allelic variant of a polymorphic region of a 5-lipoxygenase (5-LO) gene, where the allelic variant comprises one or more nucleotide selected from any of 3 20 or 21 base pair sequences, given in the specification, or their complement, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) an isolated nucleic acid molecule comprising a haplotype, where the haplotype comprises one or more of 5 20 or 21 base pair sequences, given in the specification, or their complements, and where the nucleic acid molecule is a 5-LO gene; (2) an isolated nucleic acid molecule comprising a 2189 base pair sequence (S1), given in the specification, or its portion, where the nucleic acid molecule comprises one or more nucleotide residues selected from an adenine at residue 1000, deleted residues 472-477 and an adenine at residue 559 of it, or their complements; (3) a kit comprising a probe or primer which is capable of hybridizing to the novel nucleic acid molecule, or the nucleic acid of (1) or (2); (4) determining if an asthma patient will be responsive to treatment with a 5-LO inhibitor or has a more or less severe asthma phenotype comprising: (a) obtaining a nucleic acid sample from the asthma patient; (b) determining the presence of an allelic variant which differs from the reference sequence of (S1); and (c) determining if the asthma patient will be responsive to treatment with a 5-LO inhibitor or has a more or less severe asthma phenotype based on the presence of an allelic variant which differs from the reference sequence of (S1), where the allelic variant comprises one or more of 5 21 or 20 base pair sequences, fully defined in the specification, or their complement; (5) selecting the appropriate drug to administer an asthma patient or identifying a patient who is a candidate for effective treatment of a 5-LO inhibitor comprising: (a) obtaining a nucleic acid sample from the asthma patient; (b) determining the presence of an allelic variant which differs from the reference sequence of (S1); and (c) selecting the appropriate drug to administer to a patient who has an inflammatory disease or disorder based on the presence of an allelic variant which differs from the reference sequence of (S1), where the allelic variant comprises one or more molecule sequences selected from a 21 or 20 base pairs sequence, both given in the specification, or their complement; and (6) determining the identity of an allelic variant of a 5-LO gene in a nucleic acid obtained from a patient, where the sample comprises a 5-LO gene sequence, comprising contacting a sample nucleic acid from the patient with a probe or primer having a sequence which is complementary to a 5-LO gene sequence, where the probe or primer is selected from any of 5 20 or 21 base pair sequences, given in the specification, or their complement.

BIOTECHNOLOGY - Preferred Nucleic Acid: The allelic variant of (I) further comprises one or more of any one of 2 21 base pair sequences,

given in the specification. (I) further comprises at least one variant Sp1 binding site or its complement. The nucleic acid of (2) further comprises one or more nucleotide residues selected from an adenine at residue 84 and at residue 137 of (S1). The nucleic acid molecule further comprises at least one non-wild-type Sp1 binding site allele or its complement. Preferred Kit: The probe or primer of the kit in (3) comprises a nucleotide sequence from 15-30 nucleotides, and is selected from any of 52 16-28 base pair sequences, given in the specification. The probe or primer is preferably labeled. Preferred Method: The allelic variant in the methods of (4) and (5) further comprises one or more of any one of 2 21 base pair sequences, given in the specification. (I) further comprises at least one variant Sp1 binding site or its complement. The drug is a 5-LO inhibitor. The inflammatory disease in the method of (5) has an inflammatory disease or disorder. The patient preferably has asthma. The determining of the identity of the allelic variant in the method of (6) comprises determining the identity of at least one nucleotide at any one of the nucleotide residues selected from residue 1000, any one of residues 472-477 and residue 559 of (S1), given in the specification. The determining further comprises sequencing the nucleotide sequence, performing a restriction enzyme site analysis, carried out by single-stranded conformation polymorphism or by allele specific hybridization or by primer specific extension or by an oligonucleotide ligation assay. The probe or primer comprises a nucleotide sequence from 15-30 nucleotides. The probe or primer is labeled.

USE - The compositions and methods of the present invention are useful for diagnosing and/or prognosing disorders associated with an aberrant inflammatory response such as asthma, bronchitis, sinusitis, ulcerative colitis, nephritis, amyloidosis, rheumatoid arthritis, sarcoidosis, scleroderma, lupus, non-allergic rhinitis, polymyositis, Reiter's syndrome, psoriasis, pelvic inflammatory disease, atopic and contact dermatitis. The nucleic acid molecules can also be useful for identifying an individual among other individuals from the same species, forensic medicine and paternity testing.

EXAMPLE - DNA samples were obtained from a population of 144 individuals and denaturing high performance liquid chromatography (DHPLC) was used to detect polymorphic regions in the human 5-LO gene. Polymerase chain reaction (PCR) products having product sizes ranging from 150-400 base pairs were generated using primers and 2 PCR reactions pooled together for the DHPLC analysis. Multiple pairs of primers were synthesized to amplify the axons and portions of regions. Genomic DNA was subjected to PCR in 25 micro-1 reactions under the following cycle conditions: 94 degrees C for 2 minutes, 35 x (94 degrees C for 40 seconds, 57 degrees C for 30 seconds, 72 degrees C for 1 minute), 72 degrees C for 5 minutes. The resulting PCR products were analyzed on a 2 % agarose gel. The identity was confirmed by digestion with a restriction enzyme and subsequent agarose electrophoresis. 22 pairs of oligomers were chosen to serve as PCR primers to amplify regions containing each of the 14 coding exons of the human 5-LO gene and eleven pairs were chosen to serve as primers to amplify the 5' upstream regulatory element. (290 pages)

L11 ANSWER 2 OF 3 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
 ACCESSION NUMBER: 2001:557185 BIOSIS  
 DOCUMENT NUMBER: PREV200100557185  
 TITLE: Association of a conserved promoter haplotype in the 5-  
**lipoxxygenase gene** with reduced levels of  
 peripheral eosinophils in Chinese patients with asthma.  
 AUTHOR(S): Barnes, G. [Reprint author]; Nolin, E. [Reprint  
 author]; Lewitzky, S. [Reprint author]; Shanahan, J.  
 [Reprint author]; Aelony, A. [Reprint author]; Roach, J.  
 [Reprint author]; Meyer, J. [Reprint author]  
 CORPORATE SOURCE: Millennium Pharmaceuticals Inc, Cambridge, MA, USA  
 SOURCE: American Journal of Human Genetics, (October, 2001) Vol.

69, No. 4 Supplement, pp. 563. print.  
Meeting Info.: 51st Annual Meeting of the American Society  
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12-16, 2001.

CODEN: AJHGAG. ISSN: 0002-9297.

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Conference; Abstract; (Meeting Abstract)  
Conference; (Meeting Poster)

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L11 ANSWER 3 OF 3 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN

ACCESSION NUMBER: 2001:894584 SCISEARCH

THE GENUINE ARTICLE: 483RD

TITLE: Association of a conserved promoter haplotype in the 5-  
**lipoxxygenase gene** with reduced levels of  
peripheral eosinophils in Chinese patients with asthma.

AUTHOR:

**Barnes G (Reprint)**; Nolin E; Lewitzky S;  
Shanahan J; Aelony A; Roach J; Meyer J

CORPORATE SOURCE:

Millennium Pharmaceut Inc, Cambridge, MA USA

COUNTRY OF AUTHOR:

USA

SOURCE:

AMERICAN JOURNAL OF HUMAN GENETICS, (OCT 2001) Vol. 69,  
No. 4, Supp. [1], pp. 563-563. MA 2241.  
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